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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/713,136 11/14/00 TUCK

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EXAMINER

HUYNH, P

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 11/05/01

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/713,136

Applicant(s)

TUCK ET AL.

Examiner

" Neon" Phuong Huynh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) Claims 11-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9. 6) ☐ Other:

DETAILED ACTION

1. Claims 1-42 are pending.
2. Applicant's election with traverse of Group I, Claims 1-10, drawn to a population of conjugate molecules, filed 8/15/01, is acknowledged. The traversal is on the grounds that (1) the restriction among Groups II, III and IV is improper since the claims recited immune modulation, (2) The claims of Group II and III do not recite treating disease, (3) the claims of groups II-IV do not require different ingredients and process steps to accomplish different endpoints, and (4) groups II-IV are all deemed to be in the same class and subclass and the search of all groups would not posed an undue burden on the examiner. Upon reconsideration and in response to applicant's election with traverse to the restriction requirement separating Group II-IV drawn to a method of modulating an immune response using the same product for treating an allergic condition, the restriction of Group II-IV is hereby withdrawn. Therefore, the requirement of Group II (now claims 11-42) drawn to a method of modulating an immune response is still deemed proper and is therefore made FINAL.
3. Claims 11-42 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a non-elected invention.
4. The drawings, filed 11/14/00, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.
5. The reference Nos. 38, 61, 70-71, 73, 80, 87, 106-107, 120-122, 127-128, 132, 146, 151, 180 and 182 on PTO 1449, filed 9/21/01 have been crossed out because the submission of a table of content is inappropriate for an IDS.
6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

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7. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a population" in claims 1-10 is indefinite and ambiguous. The term "population" as defined in the Webster's II New Riverside University Dictionary is all the organisms that make up a specific group or occur in a specific habitat. The term "population" implies heterogeneity within the population. As written, it is not clear whether the claimed population makes up of a homogeneous or a heterogeneous conjugate molecules.

The recitation of "is greater than about 1000" in claim 2 is indefinite and ambiguous. As written, it is not clear whether the "1000" is referring to the concentration of conjugate to the concentration of antigen or the amount of histamine being release from the basophiles induced by the conjugate or the amount of histamine being release from the basophiles induced the antigen.

The recitation of "about 100 to about 200" in claim 5 is ambiguous. As written, it is not clear whether the phrase "about 100 to about 200" is referring to the ratio of concentration of ISS-antigen to the concentration of antigen or it is referring to the concentration of ISS-antigen to the concentration of antigen or it is referring to the concentration of histamine release from basophiles.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/16247 publication (April 1998, PTO 1449).

The WO 98/16247 publication teaches a composition of conjugate molecule wherein the conjugate molecule comprises an antigen (IMM) such as β -gal or allergen such as Amb a I (page 19, lines 15-22, in particular) conjugated to a polynucleotide comprising an immunostimulatory sequence (ISS-PN or ISS-ODN) and a pharmaceutically acceptable excipient for modulating an immune response (See claims of the WO 98/16247, page 24, lines 9-27 bridging page 25, lines 1-9, in particular). The WO 98/16247 publication further teaches that the concentration of the conjugate to the antigen is 5: 1, which is within the range of about 3.5 to about 6 (See page 7, in

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particular). Claim 4 is included in this rejection because the extend of conjugation such as ISS-ODN conjugated to antigen (ISS-ODN-antigen) is the inherent method steps which depend on the reaction time. The shorter the reaction time, the concentration of antigen-ISS-ODN conjugate would be less. Conversely, the longer the reaction time, the more antigen-ISS-ODN would form until equilibrium is reached. Furthermore, the transitional phrase "comprising" expands the polynucleotide (ISS) to include additional nucleotides at either end. With regard to 50% inhibition of binding of antigen-specific antibody to antigen, it is an inherent property of the conjugated antigen since the process of conjugation alters the structure of said antigen. The WO 98/16247 publication further teaches that conjugate molecule such as ISS-PN, ISS-PN/IMM can shift the host cellular immune response away from the helper T lymphocyte type 2 (Th2) phenotype toward a helper T lymphocyte type 1 (Th1) phenotype and using this method to boost the immune responsiveness of a host to subsequence challenge by a sensitizing antigen without immunization can avoid the risk of Th2-mediated, immunization-induced anaphylaxis by suppressing IgE production in response to the antigen challenge. Furthermore, the conjugate molecule is especially advantageous for treatment of localized allergic response (See page 3, lines 8-23, in particular). The WO 98/16247 publication teaches allergen such as Amb a1 of ragweed pollen allergen can be conjugate to the polynucleotide comprising the immunostimulatory sequence (ISS-PN or ISS-ODN) (See page 19, lines 15-22, page 21-26, in particular). Thus, the reference teachings anticipate the claimed invention.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

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made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,225,292 (May 2001, PTO 892) in view of Hirschwehr *et al* (J Allergy Clin Immunol 101: 196-206, 1995, PTO 892).

The '292 patent teaches a composition of conjugate molecule comprising an antigen such as allergen conjugated to a polynucleotide comprising ISS-ODN oligonucleotide to modulate the host immune response to said antigen (See column 11, lines 52-67 bridging column 12, lines 25-36, in particular). The '292 patent teaches a method of making conjugated molecule for a pharmaceutical composition comprising the conjugate molecule and a pharmaceutically acceptable carrier such as sterile aqueous water (See column 13, lines 20-36, in particular). The '292 patent further teaches the ISS-ODN conjugate molecule stimulates the secretion of certain cytokines such as IL-12, IL-18, and IFNs that tends to shift the host cellular immune response to the Th1 repertoire which can be measure by the cytokine levels, the cytokine-stimulated lymphocyte proliferation, the IgG2 antibody level which are indicative of Th1 lymphocyte response. Likewise, the suppression of IgE levels is indicative of a Th1 lymphocytes response while the increase of IgG1 antibody levels is indicative of a Th2 lymphocyte response (See column 13, lines 55-67, in particular). Since ISS-ODN stimulates Th1 and thereby decreases the Th2 cytokine such as IL4, IgE production and IL-4 mediated lymphocyte proliferation, the decrease in histamine release from basophiles is within the purview of one of ordinary skill in the art at the time the invention was made since IL-4 is known to mediate the release of histamine. Again, the transitional phrase "comprising" is open-ended. It expands the polynucleotide to include additional nucleotides at either end. The ratio of the concentration of ISS-antigen conjugated to the concentration of conjugate antigen is an obvious variation of the extent of conjugation that depends on the reaction time or the initial substrate concentration. The shorter the reaction time, the concentration of antigen-ISS-ODN conjugate would be less. Conversely, the longer the reaction time, the more antigen-ISS-ODN would form until equilibrium is reached. The higher the initial concentration of the free antigen or ISS-OSN, it would drive the reaction to the right to form antigen ISS-ODN conjugate.

The claimed invention as recited in claims 3 and 6 differs from the references only by the recitation of said allergen is Amb a1.

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Hirschwehr *et al* teach ragweed pollen allergen such as Amb a1 and mugwort share common allergenic structures, which recognize by cross-reactive IgE antibodies from various individual allergic to mugwort. (See page 199, column 1, paragraph 1, in particular) and said allergens can induce comparable histamine release from basophiles (See Fig 6,, page 202, column 2 second paragraph, in particular) as well as nasal constriction (See Fig 7, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the allergen as taught by the '292 patent with the Amb a1 allergen as taught by Hirschwehr *et al* for a conjugate molecule comprising the Amb a1 allergen conjugated to a polynucleotide comprising an immunostimulatory sequence (ISS-ODN) oligonucleotide as taught by the '292 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '292 patent teaches the ISS-ODN conjugate molecule stimulates the secretion of certain cytokines such as IL-12, IL-18, and IFNs which would inhibit the production of IgE associated with allergy and thereby suppress TH2 cell activity; the ability to shift host immune responses from Th1 to Th2 and vice versa has substantial clinical significance for enhancing or controlling host immune response against allergy (See column 14, lines 10-16, column 14, lines 31-34, in particular).

13. No claim is allowed.
14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

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15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.

Patent Examiner

Technology Center 1600

November 5, 2001


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